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SHAVER EXAMINER

18N1/0208

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ART UNIT	PAPER NUMBER
1802	10

DATE MAILED: 02/08/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 11/20/95 election ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~____~~ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☑ Notice re Patent Drawing, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-19 are pending in the application.
   Of the above, claims 4-5, 7, 13 & 17-19 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-3, 6, 8-12 & 14-16 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Part III DETAILED ACTION

1. Acknowledgement is made of Applicants' election of Group I, claims 1-16, without traverese as indicated in an amendment (paper no. 7) received 8/21/95. Acknowledgement is also made of Applicants' election of group C, claims 6, 9 and, 10, drawn to a method for detecting the localization of a pathogen and Applicants' election of group B, claims 14 and 15, drawn to a transformed cell as recited in paper number 10, received December 11, 1995. Claims 4, 5, 7, 13 and 17-19 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected evention. Election was made **without** traverse in Paper Nos. 7 and 10. Claims 1-3, 6, 8-12 and 14-16 presently appear in the case.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

The drawings are considered to be informal because they fail to comply with 37 CFR 1.84(a)(1) which requires black and white drawings using India ink or its equivalent.

Photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(1) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed

for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(h), three sets of drawings or photographs, as appropriate, and, if filed under the provisions of 37 CFR 1.84(a)(2), an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> "The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee."

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Claim Rejections - 35 USC § 112

3. Claims 1-3, 8-12, and 14-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 it is unclear what is meant by the term "non-invasive". It is unclear if applicant intends non-invasive to mean any method which is non-surgical, such as endoscopy.

It is also clear what is encompassed by the term "biocompatible entity". In claims 9 and 10, applicants recite that the biocompatible entity is a pathogen. It is unclear that a pathogen should be considered "biocompatible" since the body's immune system would tend to mount a significant immune response

against said pathogen. Further, malignant cells would not seem to embody a biocompatible entity.

The term "conjugate" in claim 1 is also vague and confusing because it appears that it is encompassing two independent inventions: a transformed cell, as well as an infection-targeting moiety, i.e., a fusion protein. It is not necessary for applicant to limit claim 1 to a transformed cell; however, it is requested that applicant define the term "conjugate" in claim 1 to specifically include both embodiments.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 1-3, 6, 8-9 and 16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kuhn et al (Arch. Surg., November 1991, 126: 1398-1403).

As the term "light" may be interpreted as any form of electromagnetic radiation Kuhn et al is cited as prior art. Applicant may get around this rejection by specifying the form of light which is being used in the claimed invention, i.e., visible light.

Kuhn et al disclose radioimmunodetection using a radiolabeled monoclonal antibodies directed against at tumor-

associated antigen (carcinoembryonic antigen) as a means of external imaging of metastatic deposits in patients suspected to have recurrent colorectal cancer. Kuhn et al compare external gamma camera imaging with SPECT (planar and single-photon emission computed tomography) ability, a hand-held cesium-iodine gamma detection probe, abdominal exploration and CT scan (p. 1399, column 1, paragraph 1). The reference discloses that non-invasive radioimmunoscintigraphy using radiolabeled anti-CEA monoclonal antibodies has been used in patients with carcinoma of the colon and lung and is very effective in presurgical staging to detect extrahepatic metastases of colorectal adenocarcinoma (p. 1401, column 2). Figures 1-3 on page 1401 provide images from preoperative gamma external imaging. It is inherent that such imaging could be used overtime to track the localization of the CEA-monoclonal antibodies because cancer patients are routinely tested to track the progression or possible recurrence of the disease over long periods of time and this procedure is commonly used prior to operation.

6. Claims 1-3, 6, 8 and 11 are rejected under 35 U.S.C. § 102(b) as being anticipated by Compton et al (4,912,031).

Compton et al disclose a method for distinguishing between carcinomatous and/or precarcinomatous colo-rectal disease and histologically similar conditions due to diseases that are not carcinomatous or precarcinomatous comprising contacting colo-rectal tissue with an antibody that binds to blood group

substance H (abstract). A fluorescent or phosphorescent tagged antibody is introduced into the evacuated colon in an appropriate physiological bufffer. After sufficient incubation time to allow binding of the antibody to tissues expressing H substance, the unbound antibody can be washed out by enema with a physiological buffer such as PBS. Binding of the tagged antibody to the colonic or anal/rectal epithelium is determined by fluorescent or visible light colonscopy, employing a light source to excite the fluorescent or phosphorescent tag attached to the antibody (columns 7-8, lines 55-10). As the method recites a **non**-invasive detection method which comprises administering to a subject a conjugate of a biocompatible entity and a light-generating moiety it meets the limitations of the cited claims.

7. Claims 1-3, 6, 8-9 and 16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Horan et al (4,762,701).

Horan et al disclose a method for tracking cells in vivo and for determining in vivo cell lifetime. The cells first are labelled with a cyanine dye and then are injected into a subject and the dye is used to locate the cells. It is also disclosed that cell lifetime may be determined by measuring the rate of disappearance of the labelled cells (column 1, lines 50-60). The term "cell" is defined to include nucleated eukaryotic cells such as white blood cells, various tumor cells, other mammalian cells, and non-nucleated cells such as red blood cells and platelets (columns 2-3, lines 65-10). The invention also may be used to

determine an infection site, wherein the cyanine dye-labelled cells specifically interact with an organism (i.e., bacterium, fungus, neutrophils, etc.)infecting the subject (column 15, claims 13-15).

The reference discloses that in the in vivo cellular tracking analyses, cells are labelled with cyanine dyes that are externally detectable (See column 7, lines 15-35). By externally detectable, it is taught that the dyes would contain a nuclear magnetic resonance probe or an additional label of I-125. It also is stated that most commonly fluorescence is used to track cells in areas of the body **visible from outside the body**. Such as cells in the macula, retina, and blood vessels of the eye (column 7, lines 25-30). As the methods are considered "non-invasive", the reference is applicable as prior art.

8. Claims 1-3, 8, 11-12 and 14-16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tamiya et al (Nucleic, Acids Research, 1990, 18(4): 1072).

Tamiya et al disclose a potential method of non-invasive and continuous monitoring of gene expressinon during embryonic development. The reference discloses that pRSV DNA containing firefly luciferase gene microinjected into nuclei of MEDAKA (Oryzias latipes) oocytes shows 5 of the 17 microinjected embryos showed luciferase activity which was different from transgenic MEDAKA. Luciferase gene was detected in microinjected embryos in relation to luciferase activity. It is disclosed that MEDAKA has

a transparent embryo which is easy to observe during embryogenesis.

It would be possible to overcome this rejection by amending the claims to specifically read that imaging is performed through **non-transparent** tissue.

Allowable Subject Matter

9. Claim 10 contains subject matter allowable over the prior art of record. The prior art does not teach that **visible** light generated from **within** an **opaque** body could be imaged from the **outside**. The prior art teaches that detection methods utilizing light-generating moietites are either performed in areas of the body which are non-opaque, are performed in tissue which has been excised from the body, or are detected utilizing non-invasive methods within the body such as endoscopy and colonscopy. It appears that proper amendment of the instant claims would be sufficient to get around the 102 (b) art rejections. However, applicant would also need to overcome the § 112 second paragraph rejections set forth in item 3 above in order for the instant claims to be considered allowable.

10. Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1813 Fax number is (703) 305-7939 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer

E. Shaver whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

gcs 2/5/96

James C. Housel
JAMES C. HOUSEL 2/5/96
SUPERVISORY PATENT EXAMINER
GROUP 180